Attorney's Docket No.: 15775-029001 / 00-004 Applicant: Timothy A. Springer et al

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Amendments to the Claims:

The following amendments and cancellations to the claims are made without prejudice or disclaimer. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

Claims 1-24 (cancelled)

- (currently amended) A recombinant antibody, or an antigen binding fragment 25. thereof, which specifically binds to the open conformer of aL integrin relative to another conformer and inhibits interaction of LFA-1 integrin and a cognate LFA-1 integrin ligand a modified integrin I-domain in the open conformation.
- (currently amended) An antibody or an antigen binding fragment thereof, which 26. binds to an activation specific epitope on an integrin I-domain of αL in the open conformation defined by the E284C-E301C or K287C-K294C mutations, and inhibits interaction of LFA-1 integrin and a cognate LFA-1 integrin ligand.

(cancelled) 27 - 29.

30. (currently amended) A recombinant anti-integrin antibody, or an antigen binding fragment thereof, which specifically binds to the open conformer of an αL integrin I-domain relative to the closed conformer of an αL integrin I-domain, and inhibits interaction of LFA-1 integrin and a cognate LFA-1 integrin ligand an integrin I-domain in the open conformation.

31 - 73 (cancelled)

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31 - 73 (cancelled)

74. (currently amended) The antibody or an antigen binding fragment thereof, of claim 73 25, wherein said the modified-I-domain of an αL subunit contains is locked in the open conformation by amino acid substitutions K287C/K294C.

75. (cancelled)

- 76. (previously presented) The antibody or an antigen binding fragment thereof, of claim 25 or 30, wherein said antibody comprises a portion of a human antibody and a portion of a non-human antibody.
- 77. (previously presented) The antibody or an antigen binding fragment thereof, of claim 25 or 30, wherein said antibody is a humanized antibody.
- 78. (previously presented) The antibody or an antigen binding fragment thereof, of claim 25 or 30, wherein said antibody is a chimeric antibody.
- 79. (currently amended) The antibody or an antigen binding fragment thereof, of claim 73 25, wherein said the modified I-domain of an αL subunit contains is locked in the open conformation by amino acid substitutions E284C/E301C.
- 80. (previously presented) The antibody or antigen binding fragment thereof, of claim 25, wherein said antibody, or antigen binding fragment thereof, is identified by screening a phage display library with a modified integrin polypeptide, and isolating said antibody, or antigen binding fragment thereof.

81 - 82. (cancelled)

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83. (previously presented) An antibody, or an antigen binding fragment thereof, which binds to an integrin I-domain in the open conformation but not to an integrin I-domain in the closed conformation.

84. (currently amended) An antibody, or an antigen binding fragment thereof, which binds to an integrin I-domain of an αL integrin, the I-domain being locked in the open conformation by the substitutions E284C-E301C or K287C-K294C mutations but not to a modified integrin I-domain that is locked in the closed conformation by the substitutions K289C/K294C.

85 - 86. (cancelled)

- 87. (currently amended) The antibody or antigen binding fragment thereof, of claim 86 84, wherein the modified integrin I-domain in the open conformation comprises substitutions E284C/E301C in an αL subunit.
- 88. (currently amended) The antibody or antigen binding fragment thereof, of claim 86 84, wherein the modified integrin I-domain in the open conformation comprises a substitutions K287C/K294C in an αL subunit.

89 - 104. (cancelled)

- 105. (previously presented) The antibody or antigen binding fragment, of claim 83 that is a monoclonal antibody.
- 106. (previously presented) The antibody or antigen binding fragment, of claim 83 that is a recombinant antibody.

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107 - 109. (cancelled)

110. (currently amended) The antibody or antigen binding fragment, of claim 25, <u>26</u>, 30, or 83 that blocks interaction between an integrin and a cognate ligand.

111. (cancelled)

- 112. (previously presented) The antibody or antigen binding fragment, of claim 110, wherein the cognate ligand is ICAM-1.
- 113. (previously presented) The antibody or antigen binding fragment, of claim 110, wherein the cognate ligand is ICAM-2 or ICAM-3.
- 114. (currently amended) The antibody or antigen binding fragment, of claim <u>25, 26,</u> 30, 83, <u>or 84</u> 75, or 10 further comprising a physically linked detectable substance.
- 115. (previously presented) The antibody or antigen binding fragment, of claim 114, wherein the physically linked detectable substance comprises an enzyme, a fluorescent material, or a radioactive material.
- 116. (previously presented) The antibody or antigen binding fragment, of claim 114, wherein the physically linked detectable substance comprises a fluorescent or radioactive material.
- 117. (currently amended) The antibody or antigen binding fragment, of claim 25, <u>26</u>, <u>30</u>, or 84 further comprising a therapeutic moiety.

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118 - 121. (cancelled)

122. (currently amended) The antibody or antigen binding fragment, of any of claims claim 117 [[-121]], wherein the therapeutic moiety comprises a cytotoxin.

- 123. (currently amended) The antibody or antigen binding fragment, of any of claims claim 117 [[-121]], wherein the therapeutic moiety comprises a radioactive metal ion.
- 124. (currently amended) The antibody or antigen binding fragment, of any of claims claim 117 [[-121]], wherein the therapeutic moiety comprises a chemical therapeutic agent.
- 125. (currently amended) The antibody or antigen binding fragment, of any of claims claim 117 [[-121]], wherein the therapeutic moiety comprises a protein possessing a desired biological activity.
- 126. (currently amended) The antibody or antigen binding fragment, of any of claims claim 117 [[-121]], wherein the therapeutic moiety comprises a toxin.
- 127. (currently amended) A pharmaceutical composition comprising (i) an antibody or antigen binding fragment thereof according to claim 25, 26, 27, or 29, and (ii) a pharmaceutically acceptable carrier.
- 128. (currently amended) A pharmaceutical composition comprising (i) an antibody or antigen binding fragment thereof according to claim 30 or 83, or 84 and (ii) a pharmaceutically acceptable carrier.

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129. (currently amended) A pharmaceutical composition comprising (i) an antibody or antigen binding fragment thereof according to claim [[75]] <u>26</u>, and (ii) a pharmaceutically acceptable carrier.

130. (cancelled)

- 131. (new) The antibody or an antigen binding fragment thereof, of claim 25, wherein the open conformer is defined by the E284C-E301C or K287C-K294C mutations.
- 132. (new) The antibody or an antigen binding fragment thereof, of claim 30, wherein the open conformer is defined by the E284C-E301C or K287C-K294C mutations.
- 133. (new) A recombinant antibody, or an antigen binding fragment thereof, which binds to an integrin I-domain of an αL integrin, the I-domain being locked in the open conformation by the substitutions E284C-E301C but not to a modified integrin I-domain that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1.
- 134. (new) A recombinant antibody, or an antigen binding fragment thereof, which binds to an integrin I-domain of an αL integrin, the I-domain being locked in the open conformation by the substitutions K287C-K294C but not to a modified integrin I-domain that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1.